EXHIBIT E

PARRISH LAW OFFICES

788 Washington Road
Pittsburgh, Pennsylvania 15228-2021
www.dparrishlaw.com

412.561.6250
Fax 412.561.6253
E-mail: info@dparrishlaw.com

June 14, 2019

VIA PRIORITY MAIL
DHHS – OMHA
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Attn: Beneficiary Mail Stop
200 Public Square, Suite 1260
Cleveland, OH 44114-2316

BENEFICIARY APPEAL

RE: Request for ALJ Hearing
Beneficiary: David Christenson
5754 Clevedon Lane
Oshkosh, WI 54904
Dates of Service: 11/3/2018; 12/3/2018; 1/3/2019
HICN: 7QR9QM0QP33
Medicare Appeal No: 1-8486340738
Date of QIC Decision: June 7, 2019
Device: Tumor Treatment Field Therapy (E0766)
Supplier: Novocure, Inc.
Our Ref: 19-296

Dear Claims Coordinator:

As an authorized representative of the above-captioned Medicare beneficiary, David Christenson, I hereby appeal to an Administrative Law Judge the above-captioned decision rendered by the Qualified Independent Contractor ("QIC") C2C Innovative Solutions, Inc. for the claims submitted for tumor treatment field therapy ("TTFT") for a glioblastoma. The QIC rendered a nonsensical denial stating, "the medical documentation of the efficacy of this device is not within the usual scope and breath (sic) of current medical literature with peer acknowledgement and review." The QIC also asserts that although the DMACs acknowledged a valid reconsideration request was filed, LCD L34823 remains applicable until the DMACs retire it or issue a new LCD.

Mr. Christenson is a Medicare beneficiary who has been married for 41 years. He has two children and two grandchildren was diagnosed with a glioblastoma in 2016. He had surgery and was treated with radiation and chemotherapy. His clinician also prescribed TTFT and began using it in October 2016. During the clinical trial for newly diagnosed glioblastomas and a first recurrent, such as that of Mr. Christenson, the TTFT results were so compelling that at the interim analysis, the Data Safety Monitoring Board recommended that those not receiving TTFT be able to cross over to receive the treatment. The FDA agreed.

The published, peer-reviewed literature shows the improved clinical survival and the progression-free survival of patients who receive TTFT for their glioblastoma. TTFT for glioblastoma is included in the National Comprehensive Cancer Network ("NCCN") guidelines and is considered the standard of care for newly diagnosed glioblastoma. Hundreds of treating physicians, in all 50 states, have prescribed TTFT. TTFT is covered by all the large national payers. Medicare has paid for numerous claims for medically indistinguishable beneficiaries.

The QIC's determination does not make sense. The seminal articles showing the effectiveness of the treatment/device were published in JAMA, one of the most prestigious journals in the country based on "impact factor." JAMA is a peer-reviewed publication, thus the assertion that the documentation lacks review is belied by the evidence. Multiple peer-reviewed articles show the effectiveness of the device, to the QIC's comment regarding scope and breadth. The inclusion of TTFT in the NCCN guidelines is "peer acknowledgment and review."

Contrary to the QIC's assertion, on May 9, 2019, the DMACs have issued a draft LCD that extends TTFT coverage to GBM. Further, on May 28, 2019 the Civil Remedies Division ruled that the LCD record did not support the validity of the LCD under the reasonableness standard. TTFT meets Medicare coverage criteria and the QIC's decision fails to acknowledge the evidence showing the LCD is invalid.

Finally, Medicare coverage for Mr. Christenson has already been decided. Mr. Christenson received a favorable ALJ ruling on the prior dates of service.

Yours very truly,

Debra Parrish on behalf of
Mr. David Christenson

Enclosures:
Attachment A: Appointment of Representative Form
Attachment B: Certificate of Service

cc: Mr. David Christenson
Novocure, Inc., c/o Justin Kelly

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Pittsburgh, Pennsylvania 15228-2021
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Fax 412.561.6253
E-mail: info@dparrishlaw.com

July 5, 2019

VIA PRIORITY MAIL

Judge Scott Watson
Office of Medicare Hearings and Appeals
Cleveland Field Office
200 Public Sq., Suite 1300
Cleveland, OH 44114-2316

RE: Prehearing Brief
ALJ Appeal Nos. 1-8630709341
Appellant/Beneficiary: D. Christenson
Service: E0766
Dates of Services: 11/3/18, 12/3/18, 1/3/19
Hearing Date: Aug. 28, 2019
Our Ref. No.: 19-296

Dear Judge Watson:

Pease find attached a prehearing brief to aid in your analysis.

If you have any questions regarding the foregoing, please do not hesitate to contact me at (412) 561-6250. We appreciate your consideration.

Respectfully submitted,

Debra M. Parrish
Attorney for D. Christenson

Enclosures:
Prehearing Brief with Attachments

cc: Mr. D. Christenson

A. Background

Mr. David Christenson, a 65-year-old husband, father of two, grandfather of two, retired software developer, and Medicare beneficiary, was diagnosed with a glioblastoma in July 2015. His clinician prescribed chemotherapy, radiation, and surgery to treat his glioblastoma (GBM). Mr. Christenson's cancer showed evidence of enhancement in early 2016. Thereafter, Mr. Christenson started using the Optune device to treat his GBM. From that time through the dates of service at issue, Mr. Christenson has had stable MRIs. The supplier submitted claims for the Optune system to the relevant Durable Medical Equipment Contractor (DME MAC) which denied the claims.

The QIC denied the claims asserting "the medical documentation of the efficacy of this device is not within the usual scope and breadth of current medical literature with peer acknowledgement and review." The QIC also asserted that the studies were "not non-biased" because they were supported by Novocure, and there were few clinical trials. Finally, the QIC asserted that although an LCD reconsideration request had been deemed valid, LCD L34823 has not been revised and is still in effect. As described more fully below, the denial is inconsistent with Medicare coverage criteria and the record.

1. Glioblastoma Multiforme (GBM)

Glioblastoma is the most common form of primary brain cancer, but is still very rare (~10,000 cases annually in the U.S.). The National Institutes of Health (NIH) designate glioblastoma multiforme as a rare disease, with few treatment options. See e.g., https://rarediseases.info.nih.gov/diseases/2491/glioblastoma. GBM tumors are typically highly aggressive. Survival at initial presentation is approximately 10 months, and upon recurrence, approximately 6 months, even with aggressive chemotherapy.[1] Because it is extremely rare for glioblastoma to metastasize, it is efficient to treat the disease with regional therapy as part of the treatment strategy.

2. Optune (formerly NovoTTF-100A System)

Optune, previously known as the NovoTTF-100A System, is durable medical equipment that delivers alternating electric fields or Tumor Treating Fields to the brain. The device consists of an electric field generator which is connected to four insulated transducer arrays. The arrays are placed on the patient's scalp and deliver the Tumor Treating Fields Therapy ("TTFT") to the patient's glioblastoma. Basically, the fields slow the replication of the cancer cells or stop their growth all together. The fields may also destroy some of the cancer cells.

[1] Rulseh et al. "Long-term survival of patients suffering from glioblastoma multiforme treated with tumor-treating fields." World Journal of Surgical Oncology at 1 (2012).

Optune is FDA-approved for recurrent and newly diagnosed glioblastoma multiforme (GBM) brain tumors. On January 1, 2014, CMS classified the Optune device as DME requiring frequent and substantial servicing, which is billed under HCPCS code E0766 as a monthly rental through the duration of medical necessity. Optune has been shown to extend the lives of patients suffering from glioblastoma tumors.

B. Literature/Professional Societies

Optune is the subject of numerous peer-reviewed published studies that demonstrate the safety and efficacy of the Optune system and TTFT generally. The studies are reported in some of the most prestigious journals in our country including JAMA (the Journal of the American Medical Association). See submitted studies. Optune is included in the National Comprehensive Cancer Network (NCCN) guidelines for recurrent glioblastoma and for newly diagnosed GBM in combination with temozolomide. See submitted guidelines. The studies concluded the following:

- The final analysis of the randomized phase 3 trial (695 patients) found that the addition of Optune to standard chemotherapy treatment "resulted in statistically significant improvement in progression-free survival and overall survival" over patients that were treated with chemotherapy alone. Stupp et al. at 2315 (JAMA 2017). See also, interim analysis of 315 patients from this study (adding Optune to maintenance chemotherapy "significantly prolonged progression-free and overall survival"). Stupp et al. at 2542 (JAMA 2015).

- These important results come after a ten-year period of more than 23 randomized trials of new treatment modalities or products for glioblastoma that all "failed to demonstrate improved survival." JAMA 2017 at 2314-2315.

- Remarkably, adding Optune to traditional chemotherapy treatment "resulted in statistically significant longer deterioration-free survival in global health status, physical and emotional functioning, pain, and weakness of legs." Taphoorn et al. at E7 (JAMA Oncology 2018).

- As far back as 2012, researchers reported that in a study of 237 patients that received either Optune treatment or chemotherapy that the treatment was at least as effective as chemotherapy alone in terms of median survival, without the toxicity risks. Stupp et al. at 8-9 (European J of Cancer 2012).

To the extent the QIC denied the claim based on the lack of quantification of effectiveness of the device generally, the peer-reviewed literature shows the opposite. Indeed, the Data Safety Monitoring Board for the clinical trial for newly diagnosed glioblastoma (*and patients that suffered recurrences during the trial*) found the data so compelling, they recommended early termination and allowing patients who were not receiving the treatment to be

able to cross over and receive the treatment, deeming it unethical to withhold it. The FDA agreed. The outcomes data from this trial represents results for both newly diagnosed patients and those that suffered recurrences during the trial. Please see the attached bibliography regarding TTFT which shows numerous peer-reviewed articles published on TTFT and its clinical application. Contrast the foregoing with the exhibit list reflecting that the DMAC has not considered any of the literature or evidence that has been published in the past four years. In either event, on May 28, 2019, the Civil Remedies Division ruled the LCD record did not support the validity of the LCD under the reasonableness standard. On May 9, 2019, the DMACs issued a draft LCD extending Medicare coverage to TTFT.

A. The QIC's assertions regarding peer-acknowledgement is belied by the evidence.

The QIC asserted, "The medical documentation in support of efficacy is not within the usual scope and breadth of current medical literature with peer acknowledgement and review." Respectfully, the sentence and logic are difficult to follow. In terms of the breadth and scope of the peer-reviewed literature, a PubMed search reveals over 100 peer-reviewed articles ranging from randomized controlled trials, to case reports, to meta-analyses. The scope and breadth are particularly remarkable given the orphan status of the disease. In the past 10 years, TTFT was the only positive clinical trial and breakthrough treatment in glioblastoma. The pivotal studies were published in the Journal of the American Medical Association (JAMA), one of the most prestigious journals in the United States and one of the most cited journals in the world. Certainly, in view of the number of publications and the prestigious peer-reviewed articles that exist, it is difficult to understand the QIC's assertion that the studies do not have peer acknowledgement and review. Further, the peer-reviewed literature was and is so strong, that TTFT enjoys a level one recommendation in the NCCN guidelines for newly diagnosed glioblastoma. A cursory review of the NCCN guidelines reflects that less than ten percent of cancer treatments enjoy such "acknowledgement." Finally, based on the strength of the outcomes seen, the Data Safety Monitoring Board (DSMB) recommended early termination of the clinical trial so that those in the control arm of the clinical trial could cross over and receive treatment. This was so because it would have been unethical to withhold this life-saving treatment from the control group. Thus, the effectiveness of the treatment certainly enjoyed the "acknowledgement and review" of the DSMB and the FDA.

B. The QIC's assertions regarding the clinical trials are belied by the evidence.

The QIC asserted, "More specifically, the QIC has reviewed the peer reviewed and evidence based literature relative to clinical trials for TTFT, and has found the literature and clinical trials to be limited in number and the clinicals trial not non-biased; that is, the clinical trials were not independent, but funded by Novocure." Respectfully, the sentence and logic are difficult to follow. As noted above, GBM is an orphan disease with a difficult prognosis. More than one randomized controlled clinical trial was performed and reported in the peer-reviewed literature and more than 50 articles regarding TTFT for glioblastoma have been reported in the peer-reviewed literature. One of the seminal clinical trials resulted in multiple publications in

the Journal of the American Medical Association, one of the most prestigious journals in the United States. On March 6, 2019, the Contractor Advisory Committee (CAC) recommended Medicare coverage of TTFT.[2] The experts found that the peer-reviewed literature shows the treatment is safe and effective. The experts did not find that the studies were limited in number or biased.

With respect to the "not non-biased" assertion, it is unclear if the QIC is attempting to assert that the manufacturer's funding of the clinical trials resulted in biased publications that could not support Medicare coverage. The studies were conducted at some of the most prestigious academic institutions in the United States by academic researchers. Most of the published clinical research on a medical intervention is sponsored in the United States. Indeed, Medicare often requires industry to sponsor certain studies as a condition of Medicare coverage. A cursory review of the literature supporting most LCDs shows that they are industry-sponsored studies. Industry sponsorship does not make a peer-reviewed study, written by academic authors, "not non-biased" such that the study cannot support Medicare coverage. If such a standard applied, Medicare would be precluded from considering most of the peer-reviewed literature published with respect to a technological advancement – an absurd result.

With respect to the number of clinical trials, Appellant notes that GBM is an orphan disease with a high mortality rate. Because the treatment is so effective, the FDA deemed it unethical to continue a study that withheld such an effective treatment from those battling a fatal disease. This is consistent with the Declaration of Helsinki, paragraph 18.[3] The CAC recognized that just as the FDA deemed it unethical to continue the clinical trial, it would be unethical to even begin more clinical studies which involved withholding a proven effective treatment for a fatal disease. A "limited number" of clinical trials is common when a treatment is proven so effective for a fatal condition. After the first study determining that a tourniquet is an effective treatment to prevent people from dying from arterial bleeding, ethically, a second study cannot be conducted. Likewise, with TTFT, given the conclusive effectiveness, additional trials that withhold the treatment cannot be conducted ethically.

C. Widespread Adoption

Based on the strength of the peer-reviewed literature and the lack of medical alternatives,

[2] See https://med.noridianmedicare.com/web/jddme/policies/lcd/contractor-advisory-committee.

[3] See World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects: "When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study." The Declaration of Helsinki finds its roots in the Nuremberg Code which required informed consent for human clinical trials after the horrific experiments conducted in concentration camps during WWII. The quoted section has been interpreted to preclude continuation of a clinical trial when effectiveness has been established for a fatal illness.

the Optune system has been certified at more than 800 cancer treatment centers, and has been prescribed by over 1100 physicians in 50 states, the District of Columbia, and Puerto Rico, for over 7200 patients. Virtually every major payor in the United States covers the Optune system for individuals diagnosed with a glioblastoma. These payors include, among others, Highmark, Aetna, Anthem, Humana, Kaiser, UnitedHealthcare, Cigna, Harvard Pilgrim, Geisinger, HealthPartners, and several Blue Cross plans. TTFT is used in 59 of the 62 NCI-designated cancer centers.

Indeed, support for the effectiveness and widespread adoption of the TTFT device is illustrated in CMS' assignment of a HCPCS code to the technology. When an existing HCPCS code does not adequately describe a device, a supplier applies to the HPCPS workgroup for a new HCPCS code. The code communicates relevant coverage decisions and criteria, fee schedule amounts, and billing information. In view of the criteria required to get a new HCPCS code, it is difficult for a DME device to obtain a HCPCS code. A review of the 2016-2017 DMEPOS HCPCS application summary documents reflects that only five new HCPCS codes were established although there were 63 new-code requests.[4]

For the HCPCS workgroup to award a HCPCS code for a device, CMS must have information that shows the technology (a) is deemed safe and effective by the FDA, (b) clinical studies demonstrate its use results in a significantly improved medical outcome or a significantly superior clinical outcome, (c) it is significantly functionally or therapeutically different from already-coded DME, and (d) has achieved sufficient adoption by the relevant medical community to justify the "administrative burden" of adding a new HCPCS code. See HCPCS Decision Tree attached to the reconsideration request. Thus, CMS considers coverage criteria when awarding a HCPCS code.[5]

D. The LCD

LCD L34823 does not reflect consideration of the required elements or provide a rationale. An LCD that on its face fails to conform to the requirements of the Medicare Program Integrity Manual, Ch. 13, is not entitled to deference. Accordingly, LCD L34823 should not be applied. As noted above, the Civil Remedies Division found the LCD record did not support the validity of the LCD under the reasonableness standard.

In view of the LCD's obvious failure to reflect the peer-reviewed literature, consensus of experts, and acceptance by the relevant medical community (mandatory considerations for a valid LCD), the LCD should not be used to preclude Medicare coverage of a device that meets Medicare's coverage criteria and which is reasonable and medically necessary to treat Mr.

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[4] Revision requests were not included in the total number of code applications. June 7, 2017 and June 8, 2017 DMEPOS HCPCS Application Summaries available at: https://www.cms.gov/Medicare/Coding/MedHCPCSGenInfo/HCPCS-Application-Summaries.html.

[5] See www.ncbi.nlm.gov/PMC/articles/PMC3865619 for an article "HCPCS Coding: An Integral Part of Your Reimbursement Strategy" by Marcia Nusgart.

Christenson's GBM.

Notably, Administrative Law Judges are not bound by LCDs. 42 C.F.R. § 405.1062. Given the beneficiary's limited treatment options and the rarity of the disease, in addition to the compelling support for the effectiveness of the device as represented by clinical study outcomes, professional societies' statements and policies, the FDA's approval, and other payors' policies, Appellant believes the LCD should not be deferred to for Mr. Christenson's claims.

E. Collateral Estoppel

Mr. Christenson previously litigated the issue of coverage of his TTFT treatment and coverage was ordered. That is, after a full and fair opportunity to litigate the issue, coverage was ordered finding the TTFT was safe and effective and medically reasonable and necessary for Mr. Christenson - twice. The Secretary chose not to appeal those decisions and they have become final. The Secretary is barred by the doctrine of collateral estoppel/issue preclusion from re-litigating those issues with respect to Mr. Christenson. As noted by a unanimous Supreme Court:

> We have long favored application of the common-law doctrines of collateral estoppel (as to issues) and res judicata (as to claims) to those determinations of administrative bodies that have attained finality. When an administrative agency is acting in a judicial capacity and resolves dispute issues of fact properly before it which the parties have had an adequate opportunity to litigate, the courts have not hesitated to apply res judicata to enforce repose. Such repose is justified on the sound and obvious principle of judicial policy that a losing litigant deserves no rematch after a defeat fairly suffered, in adversarial proceedings, on an issue identical in substance to the one he subsequently seeks to raise. To hold otherwise would, as a general matter, impose unjustifiably upon those who have already shouldered their burdens, and drain the resources of an adjudicatory system with disputes resisting resolution. The principle holds true when a court has resolved an issue, and should do so equally when the issue has been decided by an administrative agency, be it state or federal, which acts in a judicial capacity.

See Astoria Federal Savings and Loan Assoc. v. Solimino, 501 U.S. 104, 107-8 (1991) (internal citations and quotations omitted). The application of issue preclusion would not work as basic unfairness against the Secretary and there are no special circumstances that would make it unfair to apply the doctrine. As a result, the Secretary is barred by collateral estoppel from re-litigating those issues with respect to Mr. Christenson and coverage should be ordered.

F. Reimbursement Amount

If Medicare coverage is found, payment for DME is made under a regulation, 42 C.F.R. §414.210(a), which states that:

> *. . . Medicare pays for [DME] . . .on the basis of 80 percent of the lesser of:*
>
> *(1) the actual charge for the item; [or]*
> *(2) the fee schedule amount for the item, as determined in accordance with §§414.220 through 414.232.*

Because no fee schedule exists, payment is 80% of the amount billed. See also Medicare Appeal Council Decision for ALJ 1-178898474.

G. Conclusion

This is the technology that clinicians treating central nervous system tumors have embraced. No basis exists to deny Medicare coverage of a device that is shown in the peer-reviewed literature to be a safe and effective treatment for glioblastoma, a life-threatening condition. The Optune system was approved as safe and effective by the FDA. The peer-reviewed literature further supports its efficacy and the improved clinical outcome of patients who use the device. It is incorporated in the NCCN guidelines (considered the gold standard for cancer care), and it enjoys widespread adoption by clinicians and all the major payors in the United States based on the foregoing. The Medicare beneficiary has no reasonable medical alternatives. Mr. Christenson's survival has exceeded the average time periods outlined above, if the QIC insists on a "quantification" of the effects of the device. The claims should be approved.

Attachments:

A: May 28, 2019 CRD Order
B: May 9, 2019 draft LCD
C: Prior ALJ Decisions